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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

The primary objective of this research has been to develop a new method of imaging based on the ultrasonic vibration potential. The method has not been explored before for imaging. Research has focused on building radiofrequency amplifiers in the 0.5 to 10 MHz range that have the highest signal-to-noise ratios possible since extraction of the signal is the most critical part of the imaging system. Theoretical work has been done on modeling the signal generation which is unique to the vibration potential. Experiments have been carried out on colloidal suspensions to confirm some of the predictions of the theory. Experiments with phase contrast x-ray imaging have been carried out showing the highlighting of regions having large density gradients.

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INTRODUCTION

When ultrasound travels through a colloidal suspension, a voltage known as the ultrasonic vibration potential is generated. The effect arises from two properties of colloids. First, colloids are a suspension of charged particles surrounded by a spherically distributed "counter charge" in the fluid, which gives the solution overall charge neutrality. Second, colloidal particles, in general, will have a density different from that of the fluid. Thus, when a sound wave passes through the suspension, the motion of the particle and fluid will differ owing to their different inertias. A dense particle remains almost stationary in space with the fluid flowing back and forth around the particle. Unlike the particle, the countercharge moves with the fluid. This causes the normally spherical distribution of charge to be distorted to form a dipole. The dipoles at the sites of the particles add in phase during each half acoustic cycle giving a net polarization and hence a macroscopic voltage in the fluid over the spatial extent of the half cycle.

BODY

The theory of the ultrasonic vibration potential was given first by Peter Debye[1] in 1933. He predicted that passage of an ultrasonic wave through a solution of electrolytes would cause a voltage to be generated. Since Debye's pioneering work, it was found that colloidal suspensions could produce even larger voltages than ionic solutions. There are several reviews of the vibration potential including those by Povey[2], by Zana and Yeager[3], Babchin, Chow and Sawatzky[4] and O'Brien, Cannon, and Rowlands[5-8].

The most recent theory of the vibration potential has been given by O'Brien and coworkers[5-8]. According to his theory, the magnitude of the vibration potential generated in a colloidal suspension is proportional to the density difference between the particle and the fluid, the volume fraction of the particles, the dynamic mobility of the particle, the inverse of the conductivity, and the magnitude of the ultrasonic velocity, which depends on the sound intensity.

The goal of the research carried out here is to develop the vibration potential as a method of imaging. A key finding of the work to date is that blood gives a signal whose magnitude at 500 kHz is as large as any seen in this laboratory. The idea of using the vibration potential for imaging tumors is based on the vascularization of tumors: if a large network of vessels is present in the vicinity of a tumor, and a device that images blood is devised, then it follows that tumors can be detected with the device. Quantitative work is in progress.

Insofar as imaging is concerned the signal detected in a voltage receiver S(t) generated by an ultrasonic burst of finite duration with velocity v(x,t) in a one-dimensional geometry is given by

$$S(t) = k\int c(x)v(x,t)dx \qquad (1)$$

where c(x) is the concentration of the colloid in space, k is a constant, and the integration is over the extent of the pulse in space. Clearly, Eq. 1 does not consider all the factors given by O'Brien relating to frequency, particle concentration, conductivity. For the purposes of transforming the received voltage signal into an image of the presence of colloidal species, Eq. 1 is all that is required—unless multiple frequency, or other modifications of the experiment are contemplated.

Evaluation of Eq. 1 for a suspension located at the origin that extends from –L/2 to L/2 shows some unique features of vibration potential imaging that distinguish it from other imaging methods. The geometry is that of an inert medium where the sound is generated and which conducts the sound to a region with the colloid. Consider a plane wave with a Gaussian profile of the form

$$v(x,t) = v_0 \cos k(x-ct)Exp[-(x-ct)^2/\sigma^2] \qquad (2)$$

where k is the wavenumber, v_0 is a velocity, c is the sound speed, σ is the pulsewidth parameter, x is the coordinate and t is the time. For a sound burst with a spatial extent shorter than the length of the colloidal region, the wave shown below in Fig. 1 is generated.

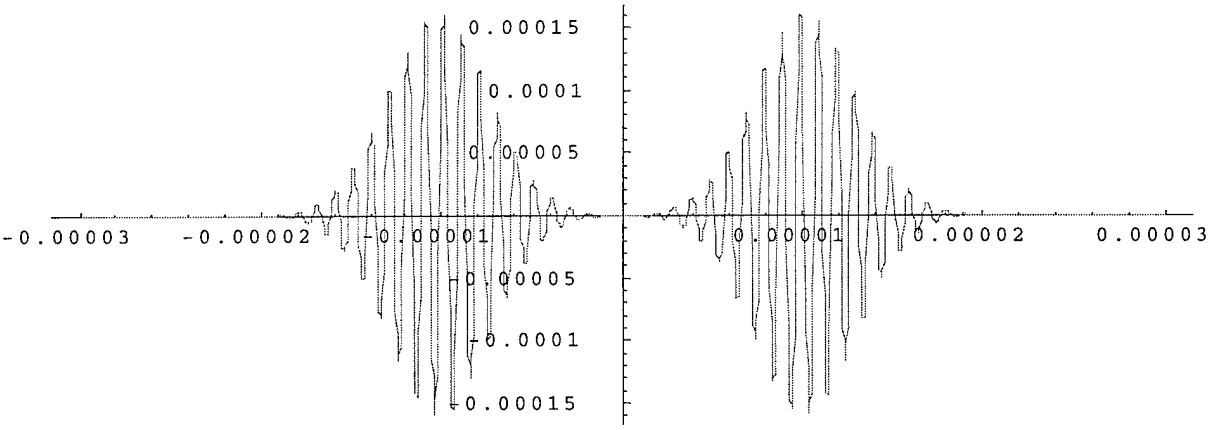

Figure 1. Vibration potential in arbitrary units versus time from the origin for c=1000 m/s, L=10 mm, σ = 4 mm, and an ultrasound beam with a frequency of 1 MHz.

Clearly, a single burst of ultrasound generates two rf signals, one when the pulse enters the region where colloid is present, and a second signal when the burst exits the region where colloid is present. The absence of a signal in the center of the trace arises because when the pulse is totally within the colloidal region the fluid velocity has both positive and negative excursions that cancel to give a vibration potential of zero. Only when the pulse enters or leaves the colloid is a signal generated. In a practical sense, imaging based on the vibration potential responds to gradients of the colloid concentration, not simply to its presence.

When the burst is long compared with the length of the colloidal region, the signal can be approximated in the center of the plot by looking at the integral

$$v(x,t) = \int \cos k(x - ct)dx$$
$$= \frac{2}{k} \sin \frac{kL}{2} \cos ckt$$

which describes a standing wave. Thus, the signal can be large or small depending on the value of sin kL/2. As Figs. 2 and 3 show, a very different character of the wave is found when k, or equivalently, the frequency, is adjusted slightly to change the value of sinkL/2.

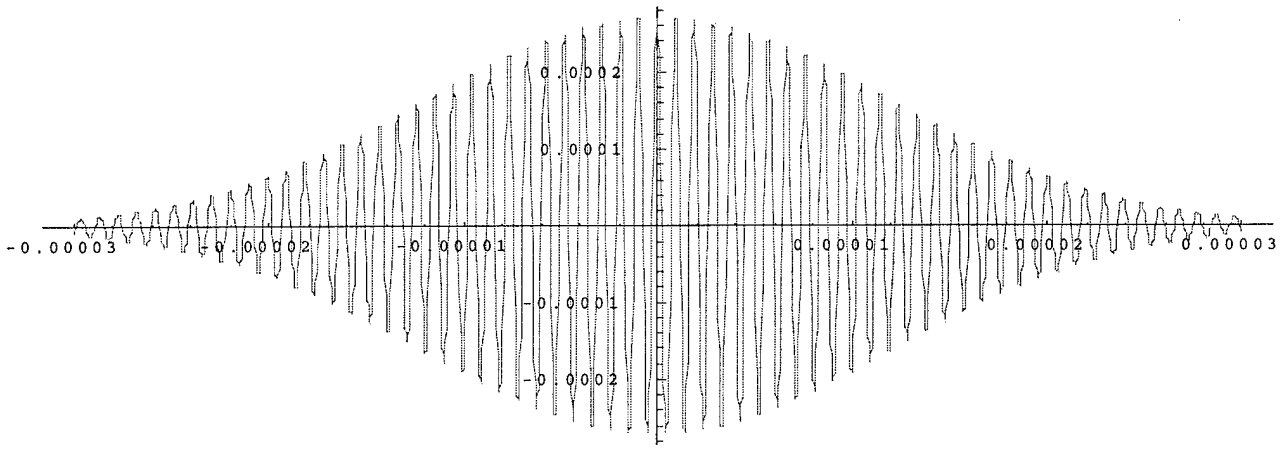

Figure 2. Vibration potential in arbitrary units versus time from the origin for c=1000 m/s, L=10 mm, σ = 15 mm, and an ultrasound beam with a frequency of 10.47 MHz giving sin kL/2=1

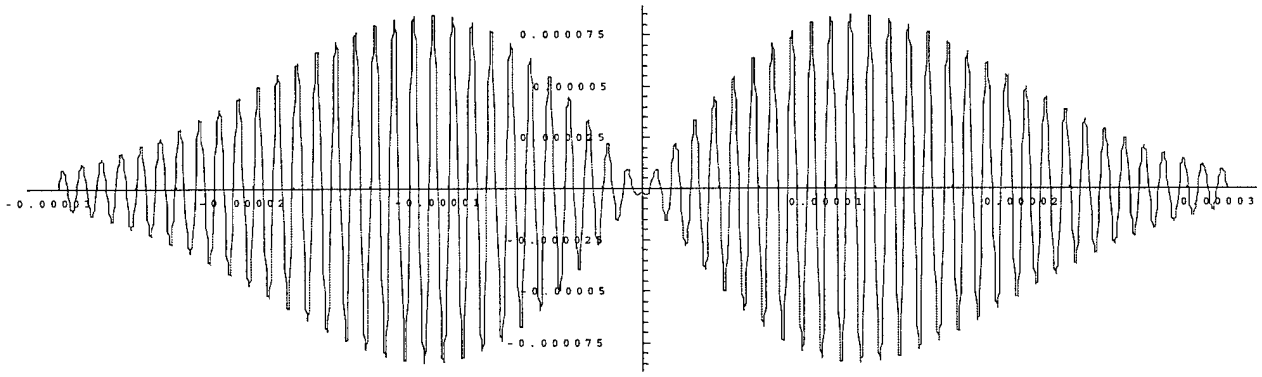

Figure 3. Vibration potential in arbitrary units versus time from the origin for c=1000 m/s, L=10 mm, σ = 15 mm, and an ultrasound beam with a frequency of 1.0 MHz giving sin kL/2=0

Note that the problem was set up with no impedance mismatch at the boundaries of the colloid—in the same experiment, conventional ultrasound would detect nothing as there is no contrast mechanism between the colloid and the surrounding medium.

Experiments have been carried out in colloidal suspensions to verify the simple theory and to determine the elementary properties of the vibration potential as it applies to imaging. A Hewlett Packard Model 8114A pulse generator was used to drive a Panametrics Model V301 500 kHz transducer to give a burst of ultrasound. The cell consisted of entrance and exit delay lines with electrodes attached at their ends that were in contact with the colloid. Conventional O-rings were used to contain the colloid. The ultrasound from the transducer was transmitted to colloid through the entrance delay line to reduce the electrical pickup in transmitting the pulse. At the far end of the cell a second delay line with a second electrode colloid was attached to the cell. This delay line lengthened the time for reflections, simplifying the signal generation.

The signals from the electrodes were fed to a narrowband amplifier specifically designed for low noise. The signals were amplified and then fed to an oscilloscope where they were signal averaged and displayed. A significant part of the effort on this project was devoted to characterizing the impedance of the cell and finding the appropriate amplifier for the first stage of amplification.

Some waveforms recorded in a silica suspension are shown below. Note that the modulation envelope of the wave closely approximated a square wave, not a Gaussian function. The vibration potential signal shown in Fig. 4 shows a case similar to that in Fig. 1 where the width of the packet σ is small compared to L. The appearance of the vibration potential signal as the packet enters and leaves the region containing the colloid is seen.

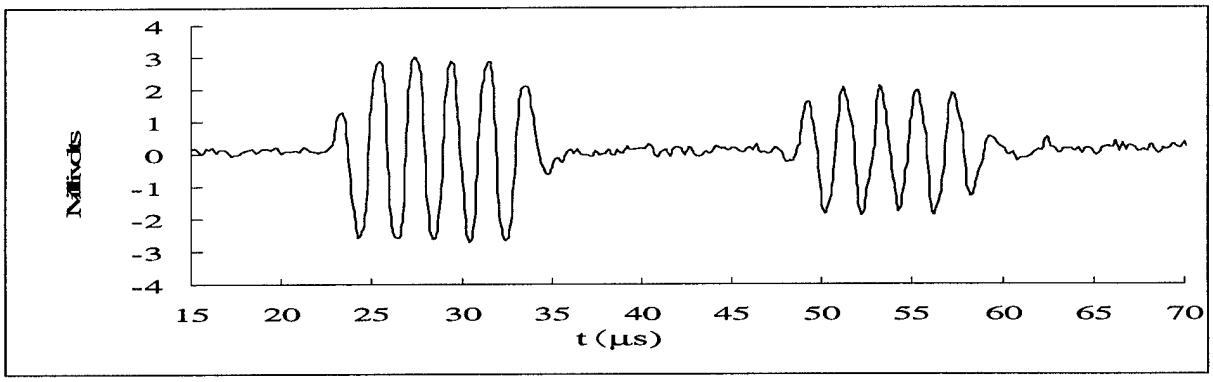

Figure 4. Voltage versus time for a burst of six pulses of 484 kHz transmitted into a silica suspension with a length of 3.81 cm.

When the number of pulses in the wave train is increased, the possibility of cancellation of the signal is present depending on the value of sin kL/2. In Fig. 5, a train of 20 pulses is sent into the same suspension as in Fig. 4. In this case, the frequency is 484 kHz, which results in a vanishing vibration potential signal as the wave train passes through the center point of the suspension.

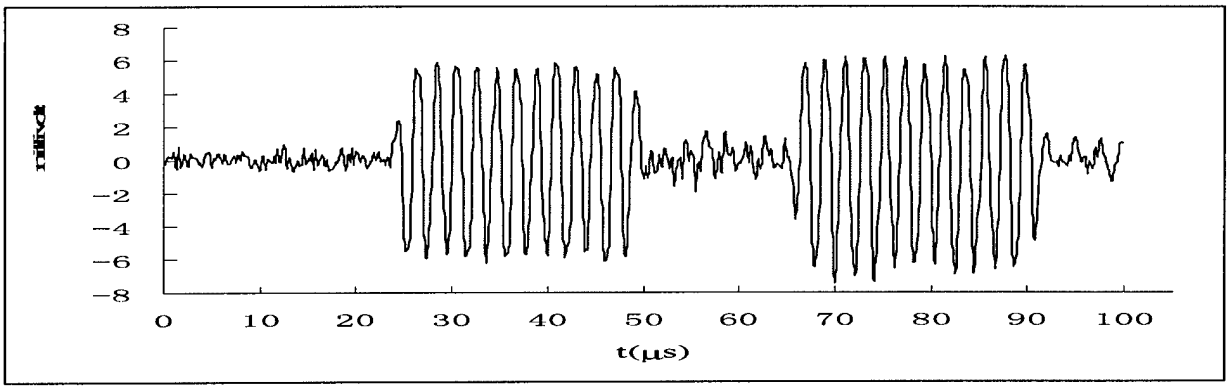

Figure 5. Voltage versus time for a burst of 20 pulses of 484 kHz transmitted into a silica suspension with a length of 3.81 cm.

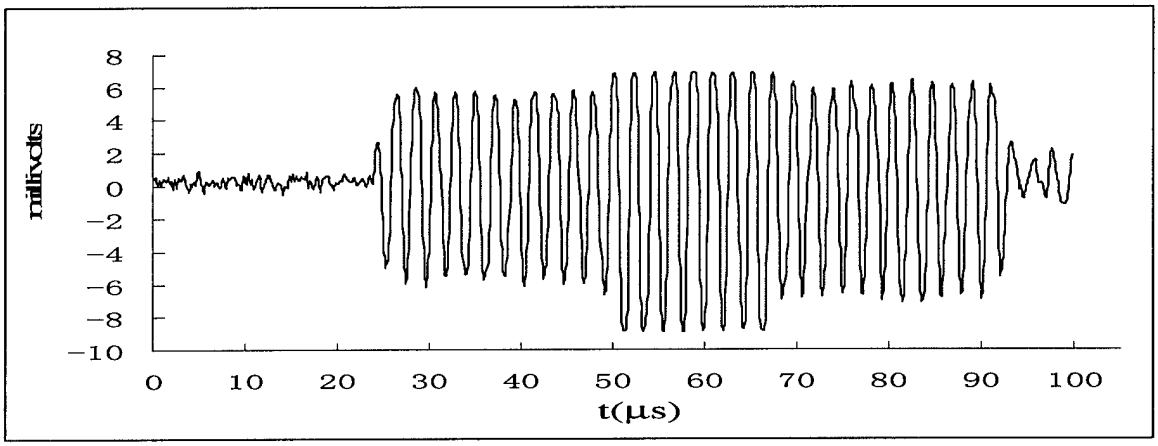

Figure 6 Voltage versus time for a burst of 20 pulses of 468 kHz transmitted into a silica suspension with a length of 3.81 cm.

By adjusting the frequency to a slightly different value, the signal for the burst in the center of the colloid is maximized, as can be seen in Fig. 6. Note in this case, there is an amplification of the signal since the impedance of the colloid differs from that of the delay line. Reflections of the wave train off of the second surface of the cell cause a standing wave to be built up in the colloid with an amplitude larger than that of the incident wave. If the delay line and colloid had the same acoustic impedance, there would be no amplification effect. Such effects may occur in actual tissue samples and cannot be ruled out. Note the inversion of the second pulse as it exits the sample in Figs. 1 and 4. The character of the wave train gives information about the dimension of the body if the signal is fitted to a model. That is, the length of the colloidal region can be found from the time dependences of the vibration potential using Eq. 1 to extract the dimensions of the colloidal region. Further work on inversion of Eq. 1 to determine c(x) from S(t) is underway. Of course, further experimental work is in progress for assembling the electronic and mechanical components of an imaging device.

Experiments have also shown that the vibration potential signal can be detected inside tissue. The experiment was to place a layer of either beef or chicken breast next to the electrodes in the cell and to look for the signals from a layer of colloid in the center of the cell. The experiments show that the meat tissue transmits the vibration potential to the electrodes and second that the meat tissue itself does not generate a vibration potential. Both of these findings are encouraging for the ultimate goal of detecting tumors which are highly vascularized.

Insofar as phase contrast imaging with the laser x-ray source is concerned, we have succeeded in preliminary in obtaining images of small objects using a microfocus x-ray tube. The goal of this project is to use the small spot size of the laser source for producing phase contrast images[9, 10] of tumors. The term "phase contrast" imaging refers to a number of methods that may be interferometric, or what is essentially an interference method. The former relies on a phase change in an x-ray beam that traverses a body where the phase change is registered by interference with an unperturbed beam. An interferometer is used in this method. The latter can be employed in a geometry where a point source of radiation is used to irradiate a body; the phase change from propagation through the body results in a deflection of the beam that interferes with an undeflected beam from the source to give an interference pattern.

The laser source available here is a 4 mJ, 40 fs beam from an amplified titanium sapphire laser that operates a roughly 1 kHz. At the focus of the laser beam a plasma is generated that emits x-rays as a result of interaction of the intense field with the plasma. The advantage of the laser x-ray source is that it more closely approximates a point source than is possible with a microfocus tube. The intensity of the laser source can be quite high, although on average it is somewhat less intense than that from microfocus tubes as a result of its low duty cycle.

We have initiated experiments using the microfocus tube since the laser is currently used for other experiments. Note the laser system is in the research laboratory of another faculty member who has agreed to collaborate on using the device in imaging experiments. The x-ray source diameter is on the order of 5 μm, which is distinctly superior to that of the best microfocus x-ray tubes. An example of a preliminary result is shown in Fig 7 where an insect leg is imaged by placing it 4 mm from the x-ray source with the detector placed 1.8 m from the source. The detector is a phosphor screen and optical system that images the fluorescence from the screen onto a liquid nitrogen cooled ccd array. The ccd camera is read by a computer and the image displayed on a screen. The magnification of the system is 45. The important feature of the phase contrast imaging is that it responds to *deflection* of the x-rays as a result of an index of refraction gradient in the specimen—absorption of the beam, on which the usual x-ray imaging relies is irrelevant. High energy photons that are only weakly absorbed can be used as well.

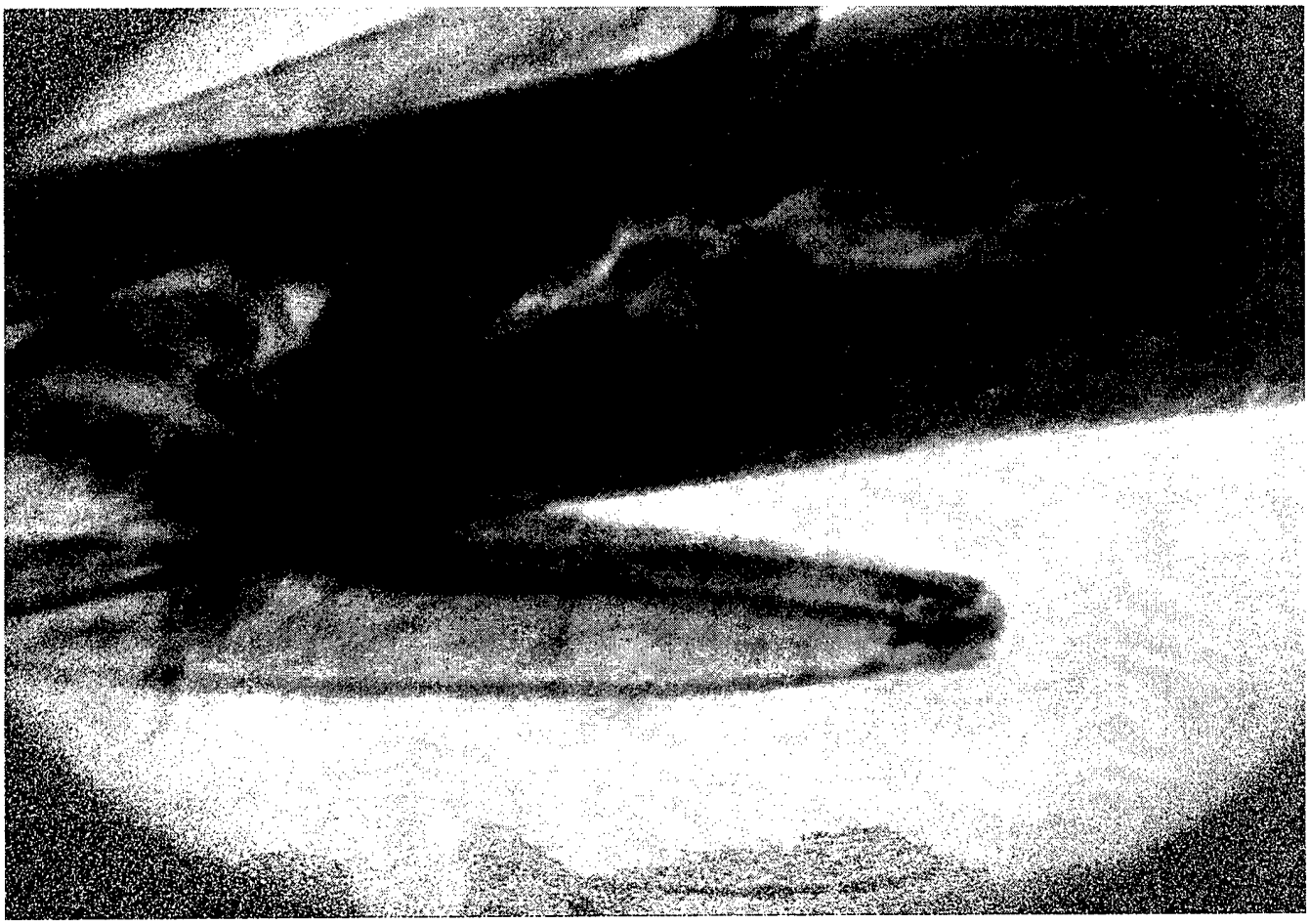

Figure 7 Phase contrast image of a mosquito thorax and leg. The sharp dark and light boundaries in the phase contrast image arise from interference of rays deflected by the index of refraction gradient with those traveling directly to the phosphor screen.

KEY RESEARCH ACCOMPLISHMENTS

The primary accomplishment for this reporting period is that the electrical characteristics of the electrochemical cell with a typical colloidal suspension has been determined and a low noise amplifier has been designed and built. The first stage of amplification is the most critical stage in the amplification of the vibration potential signal; the signal-to-noise ratio and hence the ability to detect weak signals and discern small features is wholly contingent on the signal-to-noise ratio obtained in the first amplification stage.

A rudimentary theory of how images are formed by scanning ultrasound to generate a vibration potential has been formulated. The results of simulations show how the signal depends on gradients of the colloidal concentration in space. A typical spherical colloidal volume would be expected to give two bursts of opposite phase of the vibration potential in response to a single ultrasonic burst traversing the volume in one direction. This response is fundamentally different from that seen in conventional ultrasound imaging.

Preliminary experiments have been carried out with a microfocus x-ray tube to obtain phase contrast images. The laser x-ray source available for use here has a spot size that significantly smaller than that of the best microfocus tubes; a correspondingly better phase contrast image is the expected result of the experiments.

REPORTABLE OUTCOMES

It is possible to report the results of the experiments with the vibration potential since no theory whatsoever has been published regarding imaging. However, at this point, we prefer to publish a paper with images and to include the theory and some of its consequences, and to show the relation of the vibration potential to the classic problem of a sphere in viscous fluid irradiated by a plane sound wave. The author will present an invited lecture at the NIST conference on materials properties in Boulder in June 2003.

CONCLUSIONS

The preliminary experiments that have been conducted to date with the vibration potential have shown surprising results for the way a volume of a colloidal suspension behaves when irradiated with a burst of ultrasound. The signals recorded with the new low-noise radio frequency amplifier have surprisingly large magnitudes of up to 100 μV, which is on the order of what is generated in ultrasonic imaging. It is possible to record signals through muscle tissue to detect colloidal or ionic material that is imbedded within the tissue. Muscle tissue does not generate a significant vibration potential itself. Experiments with phase contrast imaging easily highlight boundaries in tissue composition, that is, where there are gradients of density. The known high iron content of hemoglobin makes the x-ray beam deflection or "phase contrast" methods promising for detecting tumors. The use of the laser x-ray source with its small spot size should further enhance the contrast seen in phase contrast images.

At this point, no scientific or medical product is available, but the principles for such devices are being established.

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APPENDIX

No appendix is necessary